

CLAIMS

What is claimed is:

5           1.       A method for non-cellular display of 7-transmembrane receptors comprising the following steps:

- a)       incorporating an attachment scheme to a receptor;
- b)       solubilizing the receptor; and
- c)       presenting the receptor in conjunction with a support.

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2.       The method of claim 1 wherein the step of incorporating an attachment scheme to a receptor comprises incorporating at least one of the following tags from the group consisting of C-Histidine, N-Histidine, biotin, and GST tags.

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3.       The method of claim 1 wherein the step of incorporating an attachment scheme to a receptor comprises incorporating a tag into an oligonucleotide.

4.       The method of claim 1 wherein the step of incorporating an attachment scheme to a receptor comprises incorporating a tag into an FPR construct prior to amplification.

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5.       The method of claim 1 wherein the step of solubilizing the receptor comprises solubilizing by lysing cell membranes containing the receptor.

6.       The method of claim 1 wherein the step of presenting the receptor in conjunction with a support comprises presenting by affinity coupling the receptor to a particulate substrate.

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7. The method of claim 1 wherein the step of presenting the receptors in conjunction with a support comprises presenting on a support comprising at least one substrate selected from the group consisting of silica bead substrates, latex bead substrates and other bead substrates appropriate for flow cytometry.

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8. The method of claim 7 wherein the step of presenting the receptors in conjunction with a support comprises presenting on a support comprising a  $\text{Ni}^{2+}$  silica bead.

9. The method of claim 1 wherein the step of presenting the receptors in conjunction with a support comprises presenting a fluorescently labeled receptor.

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10. The method of claim 1 further comprising the step of (d) presenting at least one ligand to bind to the receptor.

11. The method of claim 10 wherein the step of presenting at least one ligand to bind to the receptor comprises presenting at least one fluorescently labeled ligand.

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12. The method of claim 10 wherein the step of presenting at least one ligand to bind the receptor comprises presenting a library of ligands.

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13. The method of claim 10 wherein the step of presenting at least one ligand to bind the receptor comprises presenting at least one ligand on a support.

14. The method of claim 10 wherein the step of presenting at least one ligand to bind to the receptor comprises presenting at least one ligand associated with a magnetically labeled support.

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15. The method of claim 10 further comprising the step of (e) combining the receptor and ligand to accomplish binding.

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16. The method of claim 15 further comprising the step of (f) sorting the bound receptor ligand pairs by fluorescence.

17. The method of claim 16 wherein the step of sorting the bound receptor ligand pairs by  
5 fluorescence comprises sorting the bound receptor ligand pairs by flow cytometry.

18. The method of claim 17 wherein the step of sorting the bound receptor-ligand pairs by flow cytometry comprises sorting the bound receptor-ligand pairs by size.

10 19. The method of claim 16 further comprising the step of (g) sorting the bound receptor-ligand pairs by magnetic field.

20. The method of claim 10 further comprising the step of (h) presenting a molecule to block the binding of the receptor with the ligand.

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21. The method of claim 20 wherein the step of presenting a molecule to block the binding of the receptor with the ligand comprises presenting at least one molecule selected from the group consisting of soluble and bead-bound molecules.

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22. The method of claim 20 wherein the step of presenting a soluble molecule to block the binding of the receptor with the ligand comprises presenting at least one drug to block the binding of the receptor with the ligand.

23. The method of claim 1 wherein the step of presenting the receptors in conjunction with a  
25 support comprises presenting the receptors in conjunction with a micelle.

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24. A method for ligand interaction analysis and drug discovery comprising the following steps:

- a) presenting a receptor within a micelle;
- b) presenting a ligand on a bead to associate with the receptor;
- 5 c) presenting a molecule to be studied to displace the receptor from the ligand; and
- d) measuring the resonance energy transfer resulting from the displacement.

10 25. The method of claim 24 wherein the step of presenting a receptor within a micelle comprises presenting a receptor within a micelle by incorporating a receptor into a micelle.

26. The method of claim 24 wherein the step of presenting a receptor within a micelle comprises presenting a solubilized receptor within a micelle.

15 27. The method of claim 26 wherein the step of presenting a receptor within a micelle comprises presenting a receptor tethered to a platform comprising at least one support selected from the group consisting of an affinity tag and a phospholipid bilayer.

20 28. The method of claim 24 wherein the step of presenting a receptor within a micelle comprises presenting a receptor within a micelle associated with at least one fluorescent acceptor.

29. The method of claim 28 wherein the step of presenting a receptor within a micelle comprises presenting a receptor within a micelle associated with at least one fluorescent acceptor  
25 selected from the group consisting of rhodamine, Texas Red and Fast Di-I.

30. The method of claim 24 wherein the step of presenting a receptor within a micelle comprises presenting a receptor having an acceptor for its own fluorescence.

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31. The method of claim 24 wherein the step of presenting a receptor within a micelle comprises presenting a receptor within which fluorescence is incorporated.

32. The method of claim 24 wherein the step of presenting a ligand on a bead to associate with the receptor comprises presenting a ligand conjugated to a fluorescent donor.

33. The method of claim 32 wherein the step of presenting a ligand on a bead to associate with the receptor comprises presenting a ligand conjugated to fluorescein.

34. The method of claim 33 wherein the step of presenting a receptor within a micelle comprises presenting a receptor associated with a GFP chimera.

35. The method of claim 24 wherein the step of presenting a receptor within a micelle comprises presenting a receptor associated with a fluorescence donor.

36. The method of claim 35 wherein the step of presenting a ligand on a bead to associate with the receptor comprises presenting a ligand associated with a fluorescent acceptor.

37. The method of claim 24 wherein the step of presenting at least one molecule to be studied to displace the receptor from the ligand comprises presenting a soluble molecule.

38. The method of claim 24 wherein the step of presenting at least one molecule to be studied to displace the receptor from the ligand comprises presenting a library of molecules.

39. The method of claim 38 wherein the step of presenting at least one molecule to be studied to displace the receptor from the ligand comprises presenting a library of drug molecules.

40. The method of claim 38 wherein the step of presenting at least one molecule to be studied to displace the receptor from the ligand comprises presenting a library of molecules on a support.

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41. The method of claim 40 wherein the step of presenting at least one molecule to be studied to displace the receptor from the ligand comprises presenting a library of molecules on a bead.

5 42. The method of claim 24 further comprising the step of (e) detecting ligand binding to receptor using resonance energy transfer (RET).

43. The method of claim 42 wherein the step of detecting ligand binding to receptor using resonance energy transfer (RET) comprises detecting ligand binding using at least one detection device  
10 selected from the group consisting of a flow cytometer, a plate reader, a spectrofluorometer, and any other fluorescence detector.

44. The method of claim 42 wherein the step of detecting ligand binding to receptor using resonance energy transfer comprises detecting using RET between the fluorescent donor and the  
15 fluorescent acceptor.

45. The method of claim 43 wherein the step of measuring the resonance energy transfer resulting from the displacement comprises measuring a diminished RET signal.

20 46. The method of claim 24 further comprising after step (b) step (f) exposing the receptor to G-protein.

47. A drug discovered by the process comprising the following steps:  
a) presenting a receptor within a micelle;  
25 b) presenting a ligand on a bead to associate with the receptor;  
c) presenting the drug to be studied to displace the receptor from the ligand; and  
d) measuring the resonance energy transfer resulting from the  
displacement.

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